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Depression Symptom Ratings in Geriatric Patients with Bipolar Mania

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Abstract

Objective—Given the paucity of information available regarding standardized ratings of depression symptoms in bipolar manic states, and in particular those in older adults, we explored depression ratings in symptomatic participants in a multicenter study of treatment of bipolar I disorder in late life.

Methods—Baseline data was obtained from the first 100 patients enrolled in an NIMH-funded, 9-week, randomized, double-blind RCT comparing treatment with lithium or valproate in patients

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aged 60 years and older with Type I Bipolar mania or hypomania. This multi-site study was conducted at six academic medical centers in the United States and enrolled inpatients and outpatients with a total Young Mania Rating Scale (YMRS) score of 18 or greater. Depressive symptoms were evaluated with the Hamilton Depression Rating Scale (HAM-D) and the Montgomery Asberg Depression Rating Scale (MADRS). The criterion for at least moderate bipolar depressive symptoms was the European College of Neuropsychopharmacology (ECNP) Consensus Meeting definition of HAM-D 17 total score > 20.

Results—Eleven percent of patients had mixed symptoms defined by depression scale severity according to ECNP criterion. In the overall sample total scores on the two depression scales were highly correlated. Total YMRS scores of this mixed symptom group were similar to the remainder of the sample.

Conclusions—These preliminary findings suggest that moderate to severe depressive symptoms occur in about one in ten bipolar manic elders. Future studies are needed to further evaluate symptom profiles, clinical correlates, and treatments for bipolar older adults with combined manic and depressive symptoms.

Keywords

Bipolar disorder; geriatrics; elderly; depression; rating scales

INTRODUCTION

Bipolar disorder (BD) is a serious and chronic mental disorder characterized by periods of mania, hypomania, mixed episodes and depressive episodes. Depressive symptoms are particularly disabling for individuals with BD, occurring over a greater proportion of an individual's life compared to manic symptoms, and being associated with substantial psychosocial impairment and reduced quality of life, as well as increasing risk for suicide (Gutierrez-Rojas *et al.*, 2008; Judd *et al.*, 2005; Valtonen *et al.*, 2005).

Many individuals with bipolar mania experience admixtures of manic and depressive symptoms (Cassano *et al.*, 1999; Gonazales-Pinto *et al.*, 2007; Cassidy *et al.*, 2008). These patients have been reported to have more severe and refractory manic illness, more frequent/intense irritability, agitation and anxiety, and more frequent psychotic features (Akiskal *et al.*, 1998; Cassidy *et al.*, 2008). Patients with combinations of symptoms have also been reported to have higher rates of suicidal ideation and suicide attempts, greater prevalence in women, younger age of bipolar illness onset, and higher rates of substance abuse and of family history of mood disorders compared to other patients with mania (Cassidy *et al.*, 2008, Gonzalez-Pinto *et al.*, 2007; McElroy *et al.*, 1992; Akiskal *et al.*, 1998; Azorin *et al.*, 2009).

Issues surrounding sub-typing of manic states are complex, and there is no clear consensus regarding categorization of mixed manic states (Cassidy *et al.*, 2008; Akiskal *et al.*, 1998). In young bipolar patients, stringently defined dysphoric mania, which requires a full spectrum of depression symptoms, has been reported to occur in approximately 7% of manic populations, while more broadly-defined dysphoric states can occur in nearly 40% of manic patients (Akiskal *et al.*, 1998). The DSM-IV characterization of bipolar mixed episode features include time duration of one week and requirement that the individuals meet formal diagnostic criteria for both a manic episode and a major depressive episode (American Psychiatric Association, 2000), however severity criteria beyond overall functional status are not clearly articulated in the DSM definition of dysphoric manic states.

The relationship of age to concomitant depressive symptoms in manic states has also been unclear. While early reports and clinical descriptions suggested that mixed symptom presentations increase with age (Spar *et al.*, 1979; Kraepelin, 1921), other reports note lower rates of mixed states with age (Shurhoff *et al.*, 2000). A review of studies on late-life bipolarity concluded that there was little difference in the prevalence of mixed states in older compared to younger patients (Depp and Jeste, 2004). Broadhead and Jacoby (1990) found no significant differences between younger versus older individuals in a study of the rating scale items including dysphoric mood in patients with mania.

There is remarkably little information available regarding standardized ratings of depressive symptoms in geriatric bipolar mania (Young *et al.*, 2007). In fact, that is the case with younger patients as well (Martinez-Aran *et al.*, 2008). A recent publication called for greater precision in bipolar outcomes assessment, and highlighted the paucity of data obtained with depression rating scales in treatment trials of patients with combined manic and depressive features (Martinez-Aran *et al.*, 2008). Although potential limitations of the Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1960) in geriatric populations have been discussed (Berk *et al.*, 2004; Linden *et al.*, 1995), the HAM-D is still widely used in geriatric treatment studies. Reports focused on late-life bipolar disorders have used either the HAM-D (Gildengers *et al.*, 2005; Sajatovic *et al.*, 2008) or the Montgomery Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) to assess depressive symptoms (Sajatovic, *et al.*, 2008a). However, to the best of our knowledge, comparisons between depression and mania severity ratings using standardized mood rating scales in geriatric bipolar samples have not been reported. Severity of specific symptoms, for example suicidality or severe psychomotor agitation, is often the driving factor in treatment decisions, and thus is of substantial clinical importance.

We examined depression ratings and other selected characteristics in a preliminary sample of patients participating in a randomized controlled trial (RCT) of treatment of geriatric Type I bipolar mania. We assessed the proportion of patients with at least moderate depression severity by ECNP criterion (Goodwin *et al.*, 2008) and their demographic and clinical characteristics. Additionally, we examined the association of HAM-D, MADRS and YMRS scores in bipolar manic elders. We expected that HAM-D and MADRS scores would be positively associated. Finally, we compared the association between HAM-D and MADRS ratings to that described in geriatric unipolar depressed patients (Heo *et al.*, 2007).

METHODS

This is a baseline data analysis of the first 100 individuals enrolled in an on-going, 9-week, randomized, double-blind RCT that was designed to compare the tolerability and efficacy of treatment with lithium or valproate in patients age 60 years and older with Type I Bipolar disorder, mania, mixed-manic episode or hypomania as confirmed by the Structured Clinical Interview for Axis I DSM-IV (SCID) (First *et al.*, 1995). This multi-site study is being conducted at six academic medical centers in the United States, and includes University hospitals, Veterans Administration hospitals, and private facilities. Study patients were enrolled from both inpatient and outpatient settings. Participants had at least moderate manic symptoms as defined by a Young Mania Rating Scale (Young *et al.*, 1978) (YMRS) score of 18 or greater. Individuals were excluded who had chronic psychotic conditions such as schizophrenia or schizoaffective disorder based upon clinical interview and confirmed with SCID, contraindications to either lithium or valproate or a history of non-response to adequate trial of lithium or valproate, active substance dependence, mood disorders due to a general medical condition or treatment, rapid cycling, diagnosis of dementia, inability to communicate in English, significant sensory impairments, recent history of cardiovascular event or stroke, or were deemed to be at high risk for suicide.

Depressive symptom severity, which was not a criterion for the sample selection, was documented with the GRID version of the HAM-D (Kalai *et al.*, 2002) and the MADRS (Montgomery and Asberg, 1979). Internal consistency (alpha coefficient) for the HAMD has been reported to range from .48 in settings without training to 0.92 with intensive training such as is generally the case for clinical trials (Kobak 2004). For the MADRS, correlations between each item and the remaining items have been reported to range from 0.12 (reduced appetite) to 0.84 (apparent sadness) (Montgomery 1979).

Other assessments in this analysis included demographic information, use of health aide or live-in help, past suicide attempt history, age of illness onset, medical comorbidity (Cumulative Illness Rating Scale—Geriatric Version; CIRS-G) (Miller *et al.*, 1992), cognitive status (Mini Mental State Examination; MMSE) (Folstein *et al.*, 1975) and Global Assessment of Functioning (American Psychiatric Association 2000). The overall study description and rationale have recently been published and describe study methods in greater detail (Young *et al.*, 2010). During the study screening period, while potential study candidates were being evaluated for eligibility, patients were on a variety of psychotropic agents. However, study patients were required to be off all other psychotropic medications at baseline (randomized treatment) (Young *et al.*, 2010).

This analysis focused on ratings of depressive symptoms in all patients at baseline. The criterion for at least moderate bipolar depressive symptom ratings was the European College of Neuropsychopharmacology (ECNP) Consensus Meeting suggestion of a HAM-D 17 total score > 20 (Goodwin *et al.*, 2008).

Statistical Analysis

Statistical analyses were performed using SAS software Version 9.1. (SAS Institute, Inc., Cary, NC). Descriptive statistics were generated for baseline measures. Associations were assessed using Pearson product moment correlation coefficient and linear regression. Group comparisons were made with Chi-square analyses or Fisher's Exact Test for dichotomous variables or student t-tests with comparisons of mean scores for continuous variables.

In comparing the intercept and slope of the regression of HAM-D and MADRS scores to that described in depressed elders by Heo *et al.* (2007), we used a 2 df likelihood ratio test at the 0.05 alpha level. All statistical tests were 2-tailed. Given the exploratory nature of the study, nominal p-values are reported without correction for multiple comparisons.

RESULTS

Sample Characteristics

Selected demographic and clinical characteristics are presented in Table 1. The proportion of male and female participants was equivalent. Nearly half of the individuals were living alone at the time of study entry. During the study screening period patients were on a variety of medications including lithium (N=10, 10%), other mood stabilizers including divalproex, lamotrigine, carbamazepine (17%), antipsychotics (31%), and antidepressants (16%), although as per study protocol, all concomitant psychotropic medications were discontinued at study baseline (randomized treatment).

SCID diagnoses were current episode manic in 69 individuals, hypomanic in 14 individuals, and mixed in 17 individuals. Depressive symptom severity as measured by the HAMD-17 (mean 19.4, SD 5.9) and the MADRS (21.8, 8.6) was higher in SCID mixed patients than in those with current mania (HAMD-17 mean 7.8, SD 5.1 and MADRS mean 8.9, SD 6.1) or hypomania (HAMD-17 mean 6.4, SD 4.6 and MADRS mean 6.8, SD 4.6).

Age was weakly but significantly associated with lower depression scores in the sample (HAM-D-17: $r = -0.21$, $p < 0.032$; MADRS: $r = -0.25$, $p < 0.013$). Age was not associated with YMRS scores ($r = 0.02$, ns).

Manic Elders with At Least Moderate Depression

Eleven percent of patients in this sample had concurrent moderate to severe depressive symptoms as defined by the ECNP criterion using HAM-D 17 score. Tables 2 and 3 identify individual item mean scores on the MADRS and HAM-D 17 for both the more and less depressed groups. The patients who met the ECNP criterion had significantly higher mean scores for nearly all items on the MADRS and HAM-D-17 with the exception of items relating to appetite/weight loss, work/activities, and motor retardation.

ECNP criterion positive participants were younger (Table 1). While criterion positive patients tended to have greater history of suicide attempt, be more often male, have a home health aide, and have earlier age at onset of illness (Table 1) these differences were not statistically significant. Furthermore, when these variables were examined in a logistic regression model that included age, only age was statistically significant. While very few ECNP criterion positive participants had a manic or hypomanic SCID current episode diagnosis (3/69, 4.3% manic, 0% mixed patients), approximately half of SCID current mixed episode participants (8/17, 47%) were ECNP criterion positive.

Comparison of MADRS Ratings to HAM-D Ratings

Depression scale ratings (HAMD and MADRS) with respect to total scores were highly positively correlated ($r = 0.88$, $df = 99$, $p < 0.001$) (Figure 1). In contrast to the association between depression ratings, mania scale ratings (total YMRS scores) were not associated with depression ratings: HAM-D-17 ($r = 0.06$; ns). In other words, in these manic bipolar elders, mania severity was not apparently related to the presence of concurrent depressive symptoms.

The strength of this association between the HAMD and MADRS was similar to the correlation of 0.80 in the unipolar elderly sample by Heo and colleagues (2007). However the regression equation in this sample was $HAM-D\ 17 = 1.65 + 0.73 \times MADRS$, which differed from that $HAM-D\ 17 = -2.68 + 0.86 \times MADRS$ described in that report. The lack of fit of the Heo equation is attributable to the difference in intercepts of the regression of HAM-D on MADRS between the two samples: 1.65 ($se=0.55$; $t=3.0$; $df=98$; $p=0.003$) for our bipolar sample vs. -2.68 ($se=3.94$; $t=-0.68$; $df=23$; $p=0.51$) for the unipolar sample assessed by Heo and colleagues (2007). That is, the mean of the HAM-D adjusted for MADRS differs between the two groups. The slopes of the regression model were more similar between the two samples: 0.73 ($se=0.04$; $t=18.0$; $df=98$; $p<0.001$) for our study bipolar sample, and 0.86 ($se=0.14$; $t=6.30$; $df=23$; $p<0.001$) for the unipolar sample (Heo et al., 2007).

DISCUSSION

In this cross-sectional baseline sample of 100 Bipolar I manic elders participating in a larger treatment trial, 11% of individuals met ECNP criterion for level of depression symptom severity. This preliminary analysis provides an application of the ECNP definition of clinically important bipolar depressive symptoms in a geriatric bipolar research population. To our knowledge this is the first such application of this criterion.

The finding that bipolar manic elders with combined manic and depressive symptoms were younger than manic elders without combined symptoms is consistent with findings in mixed-age samples (Cassidy et al., 2008; Gonzalez-Pinto et al., 2007; McElroy et al., 1992;

Akiskal et al., 1998). It is not clear how this compares to differing impressions regarding overall rates of combined symptoms in aged compared to younger bipolar patients (Spar et al., 1979; Kraepelin, 1921; Depp and Jeste 2004; Broadhead and Jacoby 1990, Azorin et al., 2009). While interpretations regarding relative comparisons of severity and prevalence of depressive symptoms among younger patients can only be made cautiously given the lack of a younger patient sample in our study, an RCT of risperidone versus placebo added on to mood stabilizers, (Yatham et al., 2003) found that 7–9% of acutely manic patients (median age for risperidone treated patients = 37, range 20–63 years and median for placebo = 42, range 19–65 years) had mixed bipolar symptoms. In the RCT by Yatham and colleagues (Yatham et al., 2003) overall baseline mean on the 21-item HAMD was 8.6 and 8.2 for risperidone and placebo groups respectively.

SCID diagnoses identified 17% of bipolar manic elders in this study as mixed episode. With respect to ECNP criterion it is important to note that symptom severity by itself does not establish a DSM-IV diagnosis of mixed bipolar state. While ECNP criterion identify clinically important depressive symptoms, it is still critical to conduct a careful diagnostic assessment, which includes consideration of such factors as functional status and illness duration to determine a mixed symptom classification.

The trends for more previous suicide attempts and earlier age of onset are similar to those reported in younger/mixed-age samples (Akiskal et al., 1998; Cassidy et al., 2008; Gonzalez-Pinto et al., 2007; McElroy et al., 1992). The trend for more males in our combined symptom group contrasts with the predominance of women in a recent report regarding a large European (EMBLEM) study (Azorin et al., 2009), which also found lower YMRS scores in the combined symptom subgroup. Using EMBLEM study criteria, there were 13 bipolar elders in our sample that had combined manic and depressed symptoms. There was a trend for the more depressed patients to have more use of a home health aide or live-in help. This may relate to the debilitating effects of bipolar depression which have been well-documented in bipolar patients (Gutierrez-Rojas et al., 2008; Judd et al., 2005; Valtonen et al., 2005).

While the correlations were small and the sample age range was restricted our data suggest that older age is more likely to be associated with more “pure” mania. It is possible that these older “pure” manic patients represent a survivor cohort. Perhaps individuals with combined manic and depressive symptoms die earlier from sequelae of depression (such as suicide) or are too functionally impaired to participate in research studies.

In contrast to some reports that suggest that manic individuals with depressive symptoms have an overall more severe mania (Akiskal et al 1998; Cassidy et al., 2008), we did not find that there was any relationship between overall mania rating scale (YMRS) total scores and overall total depression rating scale scores (HAMD, MADRS). Our finding of an association between HAM-D and MADRS total is consistent with reports in both young and aged unipolar depressed patients. Khan and colleagues (2004) found that HAM-D and MADRS scores were highly related in young patients with unipolar depression. Bagby et al (2004) found that in young unipolar depressed populations correlations between the 17-item HAM-D score and the MADRS score ranged from 0.68–0.85. A meta-analysis by Heo and colleagues (2007) in elderly unipolar depressed patients also found a high correlation between baseline mean HAM-D and MADRS ratings. While the MADRS and HAM-D were closely correlated in our sample of bipolar manic elders, the numerical formula (equation) that describes the relationship between MADRS and HAM-D scores differed in y-intercept from that in depressed unipolar elders as described by Heo and colleagues (2007). The difference in the HAMD vs. MADRS equation between our sample and the unipolar sample

described by Heo and colleagues (2007) likely is due to the higher mean scores in the unipolar depressed elders.

The study findings must be considered in the context of several limitations. 1. While the overall sample size is substantial, comparisons within the sample are limited by sample size and can result in Type II errors. 2. There are limits to generalizing from findings in participants in an RCT to all elders with geriatric bipolar mania, particularly along dimensions of severity. 3. Our analysis utilized the ECNP bipolar depression criteria, which is not specifically targeted for bipolar depressed elders. 4. Our study lacks comparison groups such as younger manic patients. 5. Comparison with those studies is limited by different ages of the samples, the definition of combined symptoms used, and the limited number of patients with combined symptoms in this sample. 6. The assessment of symptoms in bipolar patients using the HAMD-17 or 24 or the MADRS may not detect some clinical features noted in bipolar patients, such hypersomnia (Hamilton, 1960; Montgomery and Asberg, 1979; Bagby *et al.*, 2004; Goodwin *et al.*, 2008; Berk *et al.*, 2004).

CONCLUSION

In summary, these preliminary findings suggest that over one in ten bipolar manic elders may have at least moderate concurrent depressive symptoms as measured by ECNP criterion. Our report provides an initial perspective on standardized ratings of depression symptoms in late-life mania and suggests that depression symptom measurements using the HAM-D and MADRS are strongly associated. In contrast, manic symptom severity ratings do not appear to be related to depressive symptom severity in manic elders. These findings can guide further studies of depression symptoms in larger samples of elderly bipolar patients; comparison with younger bipolar patients is warranted.

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Correlation of HAM-D-17 and MADRS Total Scores

Figure 1.
HAM-D-17 and MADRS Total Scores in Bipolar Manic Elders (N=100)

Table 1**Clinical Characteristics of Geriatric Patients with Type I Bipolar Mania**

	N= 100	N= 89	N= 11	
Variable	All patients	Mild Depression*	Moderate/Severe Depression**	Statistic
Age, Mean (SD) Range 60–84	68.94 (7.13)	69.46 (7.18)	64.72 (5.27)	t =−2.11; df=98; p<0.037
Gender (N, %)				Fisher's Exact p=0.162
Female	50 (50.0)	46 (51.7)	4 (36.4)	
Male	50 (50.0)	43 (48.3)	7 (63.6)	
Race (N, %)				Fisher's Exact p= 0.350
White	86 (86.0)	76 (85.4)	10 (90.9)	
Black	13 (13.0)	13 (14.6)	0 (0.0)	
Asian	1 (1.0)	0 (0.0)	1 (9.1)	
Ethnicity: Hispanic (N, %)	9 (9.0)	8 (9.0)	1 (9.1)	Fisher's Exact Test p= 0.408
Education, Mean (SD) (Range 5–25)	13.4 years (3.14)	13.3 (3.18)	14.2 (2.78)	t=−0.86; df=93; p<0.391
Living Alone (N, %)	49 (49.0)	43 (48.3)	6 (54.6)	X ² = 0.1521; df=1; p<0.697
Marital Status				Fisher's Exact test p=0.258
Currently Married	37 (37.0)	33 (37.1)	4 (36.4)	
Married	63 (63.0)	56 (62.9)	7 (63.6)	
Other				
Uses health aide or live-in help (N, %)	18 (18.0)	14 (15.7)	4 (33.4%)	Fisher's Exact test p=0.082
YMRS(baseline) (Range 18 – 47)	26.38 (6.73)	26.4 (6.45)	26.2 (9.06)	t=0.1; df=98; p<0.918
HAMD -17 GRID (baseline) (Range 0–30)	9.59 (6.81)	7.88 (4.93)	23.45 (2.84)	N/A
MADRS (baseline) (Range 0–35)	10.81 (8.13)	9.12 (6.37)	24.45 (8.141)	t=−7.3; df=98; p<.001
GAF (Range 11–71)	45.6 (14.17)	45.6 (14.35)	45.0 (13.13)	T=0.13, df=97, p=0.893
CIRS-G cumulative score (Range 0–15)	8.52 (3.85)	8.64 (3.88)	7.50 (3.57)	t=0.88; df=96; p<0.379
Age Onset Illness Range (9–81)	35.3 (18.48)	36.3 (18.33)	27.6 (18.72)	t=1.46; df=93; p<0.147
Inpatient status at Baseline N (%)	IP: 51 (51.0) OP: 49 (49.0)	IP: 45 (50.6) OP: 44 (49.4)	IP: 6 (54.6) OP: 5 (45.4)	X ² = 0.062; df=1; p=0.803
MMSE score (baseline) Range 18–30	27.4 (2.46)	27.4 (2.49)	27.4 (2.38)	t=0.04; df=98; p<0.970
Past suicide attempt N (%)	16 (16.0)	12 (13.5)	4 (36.4)	Fisher's Exact p=0.058

	N= 100	N= 89	N= 11	
Variable	All patients	Mild Depression*	Moderate/Severe Depression**	Statistic
History of Substance Abuse N (%)	38 (38.0)	32 (36.0)	6 (54.6)	$\chi^2 = 1.436$; df=1; p<0.231

* *HAM-D Score* ≥ 20

** *HAM-D Score* > 20

Table 2

HAM-D 17 Item Baseline Scores in Bipolar Manic Elders

Item #	Item Name	N= 100	N= 89	N= 11	t	p<
		All patients	Individuals with Milder Depressive Symptoms*	Individuals with Moderate to Severe Depressive Symptoms**		
1	Depressed	0.70 (0.96)	0.53 (0.80)	2.09 (1.04)	-6.58	.001
2	Feelings Of Guilt	0.71 (1.00)	0.52 (0.80)	2.27 (1.10)	-4.93	.001
3	Suicide	0.17 (0.51)	0.09 (0.33)	0.82 (1.08)	-2.64	.010
4	Insomnia Early	0.82 (0.87)	0.74 (0.85)	1.45 (0.82)	-4.9	.001
5	Insomnia Middle	0.79 (0.89)	0.65 (0.84)	1.91 (0.30)	-2.31	.023
6	Insomnia Late	0.95 (0.93)	0.88 (0.92)	1.55 (0.82)	-5.83	.001
7	Work And Activities	0.52 (0.90)	0.36 (0.77)	1.82 (0.87)	0.35	.727
8	Retardation	0.01 (0.10)	0.01 (0.11)	0.00 (0.00)	-1.88	.063
9	Agitation	0.68 (0.78)	0.63 (0.80)	1.09 (0.30)	-5.89	.001
10	Anxiety Psychic	1.36 (1.13)	1.16 (1.01)	3.00 (0.63)	-4.01	.001
11	Anxiety Somatic	1.18 (1.03)	1.04 (0.98)	2.27 (0.79)	-7.42	.001
12	Somatic Symptoms Gastrointestinal	0.26 (0.597)	0.13 (0.40)	1.27 (0.91)	-4.41	.001
13	Somatic Symptoms General	0.48 (0.69)	0.38 (0.65)	1.27 (0.47)	-3.07	.003
14	Genital Symptoms	0.08 (0.34)	0.04 (0.26)	0.36 (0.67)	-3.47	.009
15	Hypochondriasis	0.55 (0.87)	0.45 (0.75)	1.36 (1.29)	-3.18	.002
16	Loss Of Weight	0.26 (0.65)	0.19 (0.56)	0.82 (0.98)	-0.25	.804
17	Insight	0.07 (0.29)	0.07 (0.29)	0.09 (0.30)	-2.94	.004

Comparisons were made by Student t-test, df = 98

* *HAM-D Score* 20** *HAM-D Score* > 20

Table 3

MADRS Item Baseline Scores In Bipolar Manic Elders

Item #	Item Name	N= 100	N= 89	N= 11	t	p <
		All patients	Individuals with Milder Depressive Scores	Individuals with at least Moderate Depression Scores		
1	Apparent Sadness	0.73 (1.15)	0.56 (1.00)	2.09 (1.45)	-4.52	0.001
2	Reported Sadness	0.86 (1.28)	0.67 (1.09)	2.36 (1.75)	-3.32	0.001
3	Inner Tension	1.69 (1.35)	1.54 (1.32)	2.91 (0.94)	-2.79	0.006
4	Reduced Sleep	2.88 (1.82)	2.71 (1.83)	4.27 (0.91)	-8.48	0.001
5	Reduced Appetite	0.53 (1.24)	0.25 (0.83)	2.82 (1.66)	-1.51	0.135
6	Concentration Difficulties	2.05 (1.59)	1.97 (1.58)	2.73 (1.56)	-5.09	0.001
7	Lassitude	0.76 (1.24)	0.56 (1.09)	2.36 (1.29)	-6.14	0.001
8	Inability To Feel	0.30 (0.84)	0.15 (0.58)	1.55 (1.44)	-4.69	0.001
9	Pessimistic Thoughts	0.72 (1.21)	0.54 (1.07)	2.18 (1.33)	-4.36	0.001
10	Suicidal Thoughts	0.29 (0.78)	0.18 (0.56)	1.18 (1.54)	3.02	0.003

Comparisons were made by Student t-test. df = 98.